Citation:

Randi G, Ferraroni M, Talamini R, Garavello W, Deandrea S, Decarli A, Franceschi S, La Vecchia C. Glycemic index, glycemic load and thyroid cancer risk. *Ann Oncol*. 2008 Feb; 19 (2): 380-383. Epub 2007 Oct 19.

PubMed ID: 17951595

Study Design:

Case Control Study

Class:

C - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To analyze the association between glycemic index (GI) and glycemic load (GL) and thyroid cancer risk.

Inclusion Criteria:

- Cases were 399 subjects (291 women and 108 men, aged 16-72 years, median age 44 years) admitted to the major teaching and general hospitals of study areas for histologically confirmed thyroid carcinoma diagnosed no more than two years before the interview
- Of these, 274 had papillary carcinomas (or mixed papillary/follicular), 69 follicular and 56 anaplastic or other undefined histological types.

Exclusion Criteria:

- Control subjects were 617 patients (427 women and 190 men, aged 16-74 years, median age 46 years) admitted to the same network of hospitals as cases for acute non-neoplastic diseases unrelated to known or potential risk factors for thyroid carcinoma, and unrelated to long-term diet modification (15% traumas, 17% other non-traumatic orthopaedic diseases, 28% acute surgical, and 40% other miscellaneous disorders)
- Controls admitted for any hormone-related disease were explicitly excluded.

Description of Study Protocol:

Recruitment

- From 1986 to 1992, a case-control study on thyroid carcinoma was conducted in the major teaching and university hospitals in three areas of Northern Italy: The greater Milan area, the provinces of Pordenone and Padua in the northeast of Italy

- Cases were 399 subjects (291 women and 108 men, aged 16-72 years, median age 44 years) admitted to the major teaching and general hospitals of study areas for histologically confirmed thyroid carcinoma diagnosed no more than two years before the interview. Of these, 274 had papillary carcinomas (or mixed papillary/follicular), 69 follicular and 56 anaplastic or other undefined histological types
- Control subjects were 617 patients (427 women and 190 men, aged 16-74 years, median age 46 years) admitted to the same network of hospitals as cases for acute non-neoplastic diseases unrelated to known or potential risk factors for thyroid carcinoma, and unrelated to long-term diet modification (15% traumas, 17% other non-traumatic orthopaedic diseases, 28% acute surgical, and 40% other miscellaneous disorders). Controls admitted for any hormone-related disease were explicitly excluded
- Cases and controls were recruited in the same catchment areas and, despite not singularly matched, they were comparable for gender and age. Less than 5% of the subjects identified (cases and controls) refused to participate.

Design

Case-control study.

Dietary Intake/Dietary Assessment Methodology

- Trained interviewers identified thyroid carcinoma cases and controls and administered to them a structured questionnaire that included questions on sociodemographic and anthropometric characteristics, lifestyle habits (including coffee and alcohol consumption), a problem-oriented medical history, family history of thyroid disease, history of residence in endemic goiter areas and number of years, use of diagnostic and therapeutic X-rays, for female subjects, gynecologic and reproductive history and use of exogenous hormones
- The weekly frequency of consumption of 29 food items during the two years before the onset of symptoms that led to the diagnosis was also recorded, and food items included questions on intake of refined cereals, such as bread, pasta, rice and polenta, and consumption of fruit and vegetables. GI values were assigned to these items using international tables and the average daily GI was calculated by summing the products of the carbohydrate content per serving, for each food or recipe, times the average number of servings of that food per week, times its GI, all divided by the total amount of available weekly carbohydrate intake.

Blinding Used

Not applicable.

Intervention

Not applicable.

Statistical Analysis

Odds ratios (ORs), and the corresponding 95% confidence intervals (CIs) for tertiles of GI and GL were computed using unconditional multiple logistic regression models.

Two models were considered:

- In the first model, the regression equations included terms for age, education, sex, area of residence, history of diabetes, body mass index (BMI), smoking and alcohol consumption, and intake of fruit and vegetables
- The second model included also a measure of non-carbohydrate energy intake to allow for

any potential bias due to systematic over- or underreporting.

Data Collection Summary:

Timing of Measurements

1986-1992.

Dependent Variables

Thyroid cancer risk.

Independent Variables

- Glycemic index (GI)
- Glycemic load (GL).

Control Variables

None.

Description of Actual Data Sample:

- *Initial N:*
  - Cases were 399 subjects (291 women and 108 men)
  - Controls were 617 patients (427 women and 190 men)
- *Attrition (final N):*
  - Cases=399
  - Controls=616
  - One control subject was removed from the analyses because of missing values for GI and GL
- *Age:*
  - Cases: 16-72 years, median age 44 years
  - Controls: 16-74 years, median age 46 years
- *Ethnicity:* Italian
- *Other relevant demographics:* None mentioned
- *Anthropometrics:* None mentioned
- *Location:* From 1986-1992, a case-control study on thyroid carcinoma was conducted in the major teaching and university hospitals in three areas of Northern Italy:
  - The greater Milan area
  - The provinces of Pordenone
  - Padua in the northeast of Italy.

Summary of Results:

- Compared with the lowest tertile, ORs in subsequence tertiles were 1.68 and 1.73 for GI, and 1.76 and 2.17 for GL
- OR for highest tertile of GI compared to lowest was 1.70 for papillary and 1.57 for follicular thyroid cancer
- ORs for GL were 2.17 for papillary and 3.33 for follicular thyroid cancer.

Author Conclusion:

- A diet rich in refined cereals and sugar through hyperglycemia and subsequent increase in insulin demand is related to carcinogenesis of the thyroid.
- High dietary levels of GI and GL are associated with thyroid cancer risk.

Reviewer Comments:

None.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes

2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A

5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	Yes
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	N/A
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	N/A
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	No
7.1.	Were primary and secondary endpoints described and relevant to the question?	N/A
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	N/A
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	No
7.6.	Were other factors accounted for (measured) that could affect outcomes?	N/A
7.7.	Were the measurements conducted consistently across groups?	N/A
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	N/A

8.2.	Were correct statistical tests used and assumptions of test not violated?	N/A
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	N/A
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	N/A
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes